1002. *The Preparation of Sulphinylhydrazides and their Conversion into Carboxylic Acids and Carboxylic Acid Derivatives*

By P. Hope and L. A. Wiles

A number of sulphinylhydrazides, $R\cdot CO\cdot NH\cdot NSO$, have been prepared. They are readily hydrolysed to the corresponding hydrazide, and, on heating, are converted into the carboxylic acid or acid chloride.

THIONYL CHLORIDE reacts with amines to form sulphinylamines, $R\cdot NSO$,[1] and with hydrazines to give sulphinylhydrazines, $R\cdot NH\cdot NSO$.[2] Attempts to prepare sulphinylhydrazides have been confined to the reaction of benzohydrazide and thionyl chloride in the presence of pyridine.[2] This gave a solid of wide melting range, which was probably impure *N'*-sulphinylbenzohydrazide, $Ph\cdot CO\cdot NH\cdot NSO$. Recrystallisation from ethanol converted it into dibenzohydrazide, $(Ph\cdot CO\cdot NH)_2$, with separation of sulphur and sulphur dioxide. Under the same conditions toluene-*p*-sulphonylhydrazide gave ditoluene-*p*-sulphonyl trisulphide, $(p\text{-}Me\cdot Ph\cdot SO_2)_2S_3$.

We have now examined the action of thionyl chloride on a number of hydrazides. Most of them gave products which were rapidly hydrolysed in moist air, but arylacetyl sulphinylhydrazides were surprisingly stable. By varying the conditions we have also isolated various carboxylic acids, acid chlorides, and a dihydrazide. The results are summarised in Table 1.

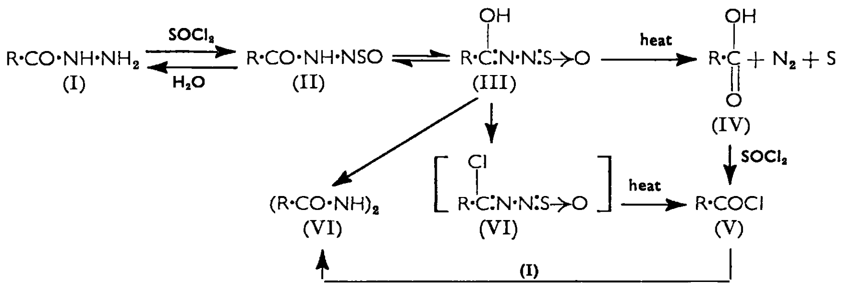
TABLE 1

Products obtained from hydrazides ($R\cdot CO\cdot NH\cdot NH_2$) and sulphinylhydrazides ($R\cdot CO\cdot NH\cdot NSO$) by the action of thionyl chloride

R	Products
Me	$Me\cdot CO\cdot NH\cdot NSO$
$[CH_2]_4\cdot Me$	$Me\cdot[CH_2]_4\cdot CO\cdot NH\cdot NSO$; $Me\cdot[CH_2]_4\cdot COCl$ [a,b]
$[CH_2]_6\cdot Me$	$Me\cdot[CH_2]_6\cdot CO\cdot NH\cdot NSO$; $Me\cdot[CH_2]_6\cdot COCl$; [a,b] $Me\cdot[CH_2]_6\cdot CO_2H$ [a,b]
$CH_2\cdot Ph$	$Ph\cdot CH_2\cdot CO\cdot NH\cdot NSO$; $Ph\cdot CH_2\cdot COCl$; [a,b] $Ph\cdot CH_2\cdot CO_2H$ [b]
CH_2-1-naphthyl	1-Naphthyl$\cdot CH_2\cdot CO\cdot NH\cdot NSO$
Ph	$Ph\cdot CO\cdot NH\cdot NSO$; $Ph\cdot COCl$; [a,b] $Ph\cdot CO_2H$; [b] $(Ph\cdot CO\cdot NH)_2$ [b] (ref. 2).
$p\text{-}C_6H_4\cdot Me$	$p\text{-}Me\cdot C_6H_4\cdot CO\cdot NH\cdot NSO$; $p\text{-}Me\cdot C_6H_4\cdot COCl$ [a,b]
$p\text{-}SO_2\cdot C_6H_4\cdot Me$	$p\text{-}Me\cdot C_6H_4\cdot SO_2Cl$ [a]

[a] From the hydrazide. [b] From the sulphinyl hydrazide.

The inter-relationship of these compounds is accounted for by the following sequence of reactions:



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[1] A. Michaelis, *Annalen*, 1893, **274**, 173.
[2] D. Klamann, U. Krämer, and P. Weyerstahl, *Chem. Ber.*, 1962, **95**, 2694.

The sulphinylhydrazide (II) may be tautomeric and, in the enol form (III), decompose to the carboxylic acid (IV), and then form the acid chloride (V). This, with excess of hydrazide (I), can give the dihydrazide (VI).

The possibility of the enol (III) being attacked by thionyl chloride to give a chlorosulphinylhydrazide (VII), which then decomposes to the acid chloride (V), we consider to be generally unlikely, since octanoic acid was isolated quantitatively from octanohydrazide. Moreover, during the reactions an initial copious evolution of nitrogen and hydrogen chloride is followed by a slower release of hydrogen chloride, the opposite of which would be expected if the sequence (III) $\longrightarrow$ (VII) $\longrightarrow$ (V) operated. It is, however, possible that this route may operate with aromatic sulphinylhydrazides in which the enol form (IIIb) is the favoured tautomer.

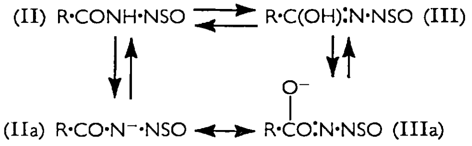
That some relationship exists between the decomposition temperature of a sulphinylhydrazide (*i.e.*, the lowest temperature at which decomposition is observed on a Kofler hot-stage apparatus), its rate of reaction with thionyl chloride, and its rate of hydrolysis is shown in Table 2.

TABLE 2

Reactions of sulphinylhydrazides

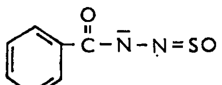
Sulphinylhydrazide	Approx. decomposition temperature (II) $\longrightarrow$ (IV)	Approx. time (days) for complete formation of acid chloride (II) $\longrightarrow$ (V)	Approx. time for hydrolysis (II) $\longrightarrow$ (I)
Benzo	65°	1	$\frac{1}{2}$ hr.
Aceto	70	—	Very rapid
Hexano	85	1	$\frac{1}{2}$ hr.
p-Toluo	100	1	$\frac{1}{2}$ hr.
Octano	110	3	3—4 hr.
Phenylaceto	130	>3	Not hydrolysed
1-Naphthylaceto	158	>3	20% in 24 hr.

Tautomerism and ionisation of sulphinylhydrazides can in general give rise to the following relationships:

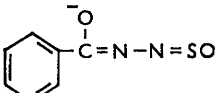


$$\begin{tikzcd}
\text{(II) R·CONH·NSO} \arrow[r, shift left] \arrow[d, shift left] & \text{R·C(OH)}\!:\!\text{N·NSO (III)} \arrow[l, shift left] \arrow[d, shift left] \\
\text{(IIa) R·CO·N}^{-}\text{·NSO} \arrow[u, shift left] \arrow[r, leftrightarrow] & \text{R·C}(\text{O}^{-})\!:\!\text{N·NSO (IIIa)} \arrow[u, shift left]
\end{tikzcd}$$

In the aliphatic series the inductive effect ($+I$) of the group R will render the carbonyl oxygen atom more negative, and will favour the anion (IIIa), and hence the formation of the carboxylic acid (IV). Thus sulphinylacetohydrazide is readily decomposed, but the effect is offset when the sulphinylhydrazide group is part of a long hydrocarbon chain, and sulphinyloctanohydrazide is more stable. This behaviour is comparable with that of the aliphatic azides, R·CON$_3$,[3] in which the lower members decompose more readily than the higher. With aromatic sulphinylhydrazides the anion (IIIb) will be favoured since it is more highly conjugated than (IIb), and sulphinylbenzohydrazide is readily converted into the acid. Sulphinyl-*p*-toluohydrazide is more stable. A similar stabilising effect has been noted for all *para*-substituted benzazides.[4]



(IIb)



(IIIb)

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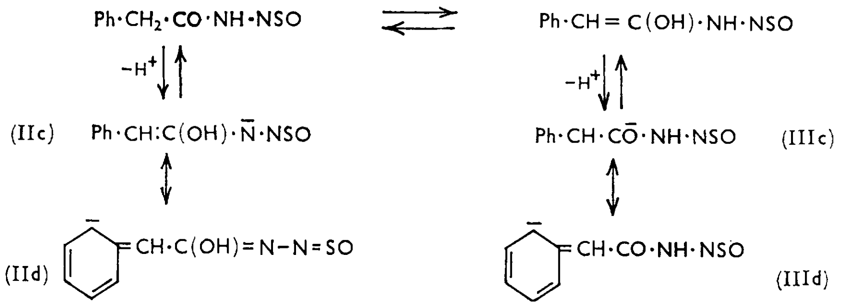
[3] P. A. S. Smith, *Org. Reactions*, 1964, **3**, 366.

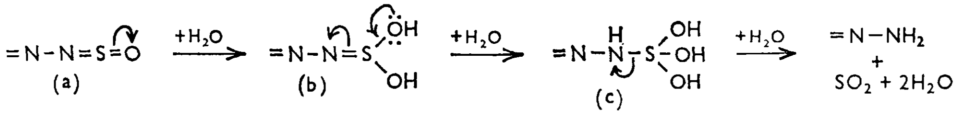
[4] Y. Yukawa and Y. Tsuno, *J. Amer. Chem. Soc.*, 1957, **79**, 5531.

With N'-sulphinylarylacetohydrazides an additional type of tautomerism and ionisation is possible, *e.g.*:



The ion (IIc) has contributory structures such as (IId) which are more conjugated than (IIId), derived from the ion (IIIc). This greater possibility of charge delocalisation gives N'-sulphinylarylacetohydrazides greater thermal stability than the benzo-compound. However, in the presence of pyridine, which favours ionisation, N'-sulphinylphenylacetohydrazide is readily decomposed to phenylacetic acid. It is noteworthy that phenylacetyl azide, $PhCH_2{\cdot}CON_3$, is stable to heat.[5]

We suggest that hydrolysis of sulphinylhydrazides occurs in the following way:



The rate of hydrolysis will depend on the extent of polarisation of the S–N bond (b). This polarisation will occur most readily in the aromatic sulphinylhydrazide anion (IIIb) where the negative charge is localised on the carbonyl oxygen atom, and N'-sulphinylbenzohydrazide is very readily hydrolysed. Conversely, an N'-sulphinylarylacetohydrazide anion will carry a proportion of the negative charge on the nitrogen atom (IIc), and this will oppose the polarisation of the S–N bond, so that these compounds are far more resistant to hydrolysis. In alkaline solution all sulphinylhydrazides, except the insoluble octano-compound, are rapidly hydrolysed.

Acid chlorides have been prepared from hydrazides by Carpino [6] using hydrogen chloride and chlorine, by reaction with sulphur monochloride,[7] and in the present work using thionyl chloride. The latter method gives very high yields of the acid chloride, possibly rather better than those obtained by Carpino, but the yields from the sulphur monochloride process are significantly lower. Production of the acid chloride using thionyl chloride is considerably slower than with hydrogen chloride and chlorine.

Benzohydrazide and thionyl chloride gave only a moderate amount of dibenzohydrazide in contrast with the excellent yield using sulphur monochloride. The product can originate in two ways, (i), by the condensation of sulphinylbenzohydrazide with benzoic acid obtained from its decomposition (equations 1 and 2), and (ii), by reaction of the hydrazide with the acid chloride (V) + (I) ⟶ (VI; R = Ph). The latter reaction is the limiting factor, since most of the benzohydrazide reacts immediately with thionyl chloride to give the sulphinyl derivative

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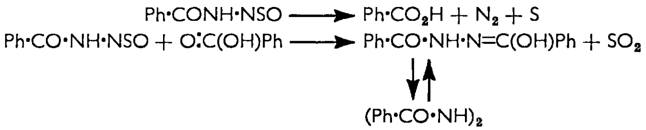
[5] T. Curtius and E. Boetzelen, *J. prakt. Chem.*, 1901, **64** (2), 314.

[6] L. A. Carpino, *J. Amer. Chem. Soc.*, 1957, **79**, 96.

[7] P. Hope and L. A. Wiles, *J.*, 1964, 5837.



$$\mathrm{Ph{\cdot}CONH{\cdot}NSO} \longrightarrow \mathrm{Ph{\cdot}CO_2H + N_2 + S} \qquad (1)$$

$$\mathrm{Ph{\cdot}CO{\cdot}NH{\cdot}NSO + O{:}C(OH)Ph} \longrightarrow \mathrm{Ph{\cdot}CO{\cdot}NH{\cdot}N{=}C(OH)Ph + SO_2}$$

$$\downarrow\uparrow$$

$$\mathrm{(Ph{\cdot}CO{\cdot}NH)_2} \qquad (2)$$

EXPERIMENTAL

The monoacyl hydrazides were obtained commercially, or were prepared by the reaction of the ester with hydrazine hydrate solution (99%).[3] M. p. and decomposition temperatures were determined on a Kofler hot-stage apparatus. Infrared spectra were measured as Nujol mulls or in carbon tetrachloride solution using a Perkin-Elmer " Infracord " spectrophotometer. In the general procedure the hydrazide (1 mole) and thionyl chloride (4 moles) were boiled under reflux in chloroform until the solution was clear. Hydrogen chloride was copiously evolved, together with some nitrogen and sulphur dioxide. Evaporation of the solution and recrystallisation from ether or light petroleum (b. p. 40—60°) gave the sulphinylhydrazide.

N′-*Sulphinylacetohydrazide*.—Acetohydrazide (3·7 g.) and thionyl chloride (14·5 ml.) were boiled under reflux in chloroform (100 ml., 1 hr.). Extraction with light petroleum gave N′-*sulphinylacetohydrazide* (4·9 g., 81·7%) as a pale yellow solid, m. p. 65—69°. It fumed in moist air, and dissolved readily in cold water with evolution of sulphur dioxide, and decomposed to acetic acid and sulphur on drying *in vacuo*.

N′-*Sulphinylhexanohydrazide*.—Hexanohydrazide (6·5 g.) and thionyl chloride (14·5 ml., were boiled under reflux in chloroform (100 ml.) for 1 hr. The oily product, dissolved in light petroleum and recrystallised, gave light brown crystals of N′-*sulphinylhexanohydrazide* (5·7 g., 65%), m. p. 33—34°. $\nu_{\text{max.}}$ 3160 (–NH), 1685 (–CO), 1460 and 1280 (–NH/–CN coupling bands),[8] 1220 (*asym* –NSO), and 1100 cm.$^{-1}$ (*sym* –NSO).[2] It hydrolysed in cold water to an oil which could not be crystallised, and dissolved readily in sodium hydroxide solution (5N) with evolution of nitrogen. Acidification gave an oil which was probably impure hexanohydrazide.

N′-*Sulphinyloctanohydrazide*.—Octanohydrazide (7·9 g.) and thionyl chloride (14·5 ml.) were boiled under reflux in chloroform (100 ml.; 1 hr.). The oily product, recrystallised from light petroleum (b. p. 40—60°) gave pink coloured plates of N′-*sulphinyloctanohydrazide* (8·2 g., 80·5%), m. p. 50°. $\nu_{\text{max.}}$ 3185 (–NH), 1695 (–CO), 1460 and 1280 (–NH/–CN coupling bands), 1215 (*asym* –NSO), and 1100 cm.$^{-1}$ (*sym* –NSO) (Found: C, 47·1; H, 7·9; N, 13·7; S, 15·7. $C_8H_{16}N_2O_2S$ requires C, 47·8; H, 8·1; N, 13·7; S, 15·2%). It decomposed slowly at ordinary temperatures, and was rapidly hydrolysed by hot sodium hydroxide solution (5N) to give octanohydrazide, m. p. and mixed m. p. 89°.

N′-*Sulphinylphenylacetohydrazide*.—Phenylacetohydrazide (3·8 g.) and thionyl chloride (7·8 ml.) were boiled under reflux in chloroform (50 ml.; 4 hr.). The solid residue (4·5 g., 92%), recrystallised from benzene, gave N′-*sulphinylphenylacetohydrazide*, white plates, m. p. 129°, $\nu_{\text{max.}}$ 3155 (–NH), 1680 (–CO), 1460 (–NH/–CN coupling band), 1215w (*asym* –NSO), and 1100 cm.$^{-1}$ (*sym* –NSO) (Found: C, 50·0; H, 3·8; N, 14·2; S, 16·3. $C_8H_8N_2O_2S$ requires C, 49·0; H, 4·1; N, 14·3; S, 16·3%). It was stable at ordinary temperatures, and was recovered unchanged after suspension in water (24 hr.). It was readily hydrolysed by sodium hydroxide solution (5N) with evolution of nitrogen. No detectable nitrogen was evolved on boiling under reflux in chloroform (12 hr.), but the recovered sulphinylphenylacetohydrazide had a lower m. p. (126°), and smelt strongly of phenylacetic acid. Repetition of this experiment with the addition of pyridine (1 ml.) gave evolution of nitrogen (20 hr.). Evaporation of the solution yielded sulphur and phenylacetic acid, m. p. 73° (lit., 76°). No unchanged sulphinylphenylacetohydrazide was recovered.

N′-*Sulphinyl*-1-*naphthylacetohydrazide*.—1-Napththylacetohydrazide (10·0 g.) and thionyl chloride (14·5 ml.) were boiled under reflux in chloroform (100 ml.; 2 hr.). The solid residue (8·6 g., 70%), recrystallised from benzene, gave N′-*sulphinyl*-1-*naphthylacetohydrazide*, m. p. 162° (decomp.), $\nu_{\text{max.}}$ 3105 (–NH), 1710 (–CO), 1455 and 1270 (–NH/–CN coupling bands), 1215 (*asym* –NSO), and 1100 cm.$^{-1}$ (*sym* –NSO) (Found: C, 59·3; H, 4·4; N, 11·4; S, 12·7. $C_{12}H_{10}N_2O_2S$ requires C, 58·5; H, 4·1; N, 11·4; S, 13·0%).

Sulphinylbenzohydrazide.—Benzohydrazide (6·8 g.) and thionyl chloride (14·5 ml.) were boiled under reflux in chloroform (100 ml.; 2 hr.). Extraction with light petroleum (40—60°)

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[8] D. Prevorsek, *Bull. Soc. chim. France*, 1958, 795.

gave *sulphinylbenzohydrazide* (7·4 g., 81%), m. p. 82° (decomp.), $\nu_{\text{max.}}$ 1720 (–CO), 1470 and 1290 (–NH/–CN coupling bands), and 1090 cm.$^{-1}$ (*sym* –NSO) (Found: C, 47·1; H, 3·5; N, 15·1; S, 16·9. $C_7H_6N_2OS$ requires C, 46·2; H, 3·3; N, 15·4; S, 17·6%). Repetition of the experiment at 20° using 3 moles of thionyl chloride to 1 mole of benzohydrazide gave benzohydrazide hydrochloride (2 moles) but only 10% yield of sulphinylbenzohydrazide. The compound decomposed on heating to give a mixture of dibenzohydrazide (m. p. and mixed m. p. 239°), benzoic acid, and sulphur. It was readily hydrolysed in cold water.

*Sulphinyl-*p*-toluohydrazide.*—*p*-Toluohydrazide (7·5 g.) and thionyl chloride (14·5 ml.) were boiled under reflux in chloroform (100 ml.; 2 hr.). Extraction with light petroleum gave *sulphinyl-*p*-toluohydrazide* (2·2 g., 83·5%), m. p. 105° (decomp.), $\nu_{\text{max.}}$ 3125 (–NH), 1670 (–CO), 1460 and 1270 (–NH/–CN coupling bands), 1210w (*asym* –NSO), and 1100 cm.$^{-1}$ (*sym* –NSO) (Found: C, 49·8; H, 4·3; N, 14·2; S, 15·9. $C_8H_8N_2O_2S$ requires C, 49·0; H, 4·1; N, 14·3; S, 16·3%). It was rapidly hydrolysed by cold water to *p*-toluohydrazide, m. p. and mixed m. p. 117°.

Formation of Acid Chlorides.—(*a*) *From sulphinylhydrazides.* The sulphinyl hydrazide (1 g.) was boiled under reflux with thionyl chloride (2 ml.) in chloroform (25 ml.) until hydrogen chloride, nitrogen, and sulphur dioxide ceased to be evolved. The solution was evaporated and the acid chloride distilled. The reactions with sulphinyloctanohydrazide, and sulphinylphenylacetohydrazide were stopped after 24 hr., and the intermediate carboxylic acid was separated by distillation:

Sulphinyl-hydrazide	Hexano-	Octano-	Octano-	Phenylaceto-	Benzo-	*p*-Toluo-
Reaction time (days)	1	1	3	1	1	1
Product	–COCl (79%)	$-CO_2H$ (49%)	–COCl (80%)	$-CO_2H$ (30%) –COCl (13%)	–COCl (77%)	–COCl (52%)

(*b*) *From hydrazides.* The hydrazide (0·05 mole) and thionyl chloride (0·2 mole) were boiled under reflux in chloroform (100 ml.) until hydrogen chloride, nitrogen, and sulphur dioxide ceased to be evolved. The solution was evaporated, the acid chloride distilled, and characterised as the amide. The use of varying proportions of benzohydrazide and thionyl chloride gave a maximum yield of benzoyl chloride (76%) with a molar ratio of 1 : 4.

Hydrazide	Hexano-	Octano-	Phenylaceto-	Benzo-	*p*-Toluo-	*p*-Toluene-sulphono-
Reaction time (days)	1	3	3	1	1	1
Yield (%) ...	73	83	83	76	95	68

Formation of Octanoic Acid from Octanohydrazide.—Octanohydrazide (7·9 g.) and thionyl chloride (14·5 ml.) were boiled under reflux in chloroform (100 ml.; 12 hr.). On distillation there was a sudden evolution of gas, probably from the decomposition of sulphinyloctanohydrazide, and octanoic acid (7·2 g., 100%) was obtained (Found: Equiv. 148. Calc. for $C_8H_{16}O_2$ Equiv., 144).

Formation of Benzoic Acid from Benzohydrazide.—Benzohydrazide (3·4 g.) and thionyl chloride (7·8 ml.) were boiled under reflux in chloroform (50 ml.; 4 hr.). Benzoic acid (0·3 g., 10%), benzoyl chloride (0·2 g., 6%), and dibenzohydrazide (0·3 g., 10%; m. p. and mixed m. p. 239°) were isolated.

Formation of Dibenzohydrazide from Benzohydrazide.—Benzohydrazide (3·4 g.) and thionyl chloride (8·2 ml., 1·05 mole) were boiled under reflux in benzene (50 ml., 24 hr.) until hydrogen chloride ceased to be evolved. On cooling, dibenzohydrazide (46·7%; m. p. and mixed m. p. 243°) crystallised.

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